

Thioctic acid enantiomers prevent central nervous system changes occurring in a model of compressive neuropathy

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Thioctic or alpha-lipoic acid (ALA) is a naturally occurring antioxidant. It has two optical isomers designated as (R+) and (S-). Naturally occurring ALA is the (R+)-isoform, but synthetic ALA available as a registered drug or as a nutraceutical is a mixture of (R+) and (S-)-isoforms. ALA has been proposed as a potential therapeutic agent in the treatment or prevention of several pathologies related to an imbalance of the oxidoreductive status. Oxidative stress may have a relevant role in the development of neurological disorders. Peripheral neuropathy is one of these disorders characterized by myelin damage and axonal degeneration causing chronic pain syndromes with allodynia, hyperalgesia, altered sensitive information processing and impaired nerve function.

The present study was designed to assess if compression of sciatic nerve, induced by loose ligation of it, is accompanied by an increased oxidative stress and by central nervous system damage. This study has also investigated the role of ALA enantiomers treatment in preventing damage related to oxidative stress. Loose ligation of the right sciatic nerve was performed in spontaneously hypertensive rats (SHR), used as a model of enhanced oxidative stress, and normotensive Wistar-Kyoto rats (WKY) used as a reference group. Animals with sciatic nerve ligation were left untreated or were treated intraperitoneally for 14 days with racemic-ALA (25 and 50 mg/Kg/day), (R+)-ALA(25 mg/Kg/day), (S-)-ALA (25 mg/Kg/day) and with the anticonvulsant agent used in treating neuropathic pain pregabalin (50 mg/Kg/day).

Loose ligation increased astrogliosis in lumbar spinal cord and in brain at the levels of primary and secondary motor and general sensory cortices. Astrogliosis is probably related to the increase of oxidative stress in the model of compressive neuropathy used. Treatment for 14 days with (R+)-thioctic acid decreased the number and size of astrocytes, racemic-ALA was less effective, whereas the (S-) enantiomer and pregabalin were without effect. Moreover, in the brain of SHR neuronal damage and decreased expression of neurofilament phosphorilated (NFP) protein was noticeable. The number of neurons and the expression of NFP were not affected by antioxidant treatment.

The present study has documented the occurrence of microanatomical changes in the central nervous system consequent to peripheral nerve damage. These changes are countered by antioxidant treatment being (R+)-thioctic acid the most effective agent. This may have consequences in terms of clinical applications.

Keywords: Neuropathy, brain, oxidative stress, antioxidant treatments